

Applicants: David M. Stern et al.  
Serial No.: 09/374,213  
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**REMARKS**

Claims 41, 44, 46 and 55-58 are pending in the subject application. No claim has been added, canceled or amended herein. Accordingly, claims 41, 44, 46 and 55-58 are still pending and under examination.

The Examiner rejected claims 41, 44, 46 and 55-58 in the Advisory Action because the model of amyloidosis in a mouse pancreas allegedly does not indicate efficacy in treating Alzheimer's disease and because allegedly, there is no art-recognized nexus between the two.

Applicants respectfully traverse the Examiner's rejection. The pending claims are drawn upon a method of inhibiting the binding of a  $\beta$ -sheet fibril to RAGE on the surface of a cell of a subject, wherein the cell is located outside the central nervous system of the subject, which comprises contacting the cell with a compound that inhibits binding of the  $\beta$ -sheet fibril to RAGE.

Applicants maintain that the mouse model for amyloidosis does indicate efficacy in treating Alzheimer's disease, and that there is an art-recognized nexus between the two. In support of their position, applicants submit Yan S. et al., "Receptor-Dependent Cell Stress and Amyloid Accumulation in Systemic Amyloidosis" Nature Medicine 6, 643-651 (2000), attached hereto as **Exhibit A**. In the abstract on page 643, Yan et al. states, in part, that "[i]n a mouse model, amyloid A accumulation, evidence of cell stress and

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expression of RAGE were closely linked. Antagonizing RAGE suppressed cell stress and amyloid deposition in mouse spleens." Yan et al. further states at page 649, column 2 that "[a]nother property of RAGE consistent with involvement of the receptor in fibrillogenic disorders is related to its induction in chronic diseases such as systemic amyloidosis, atherosclerosis, *Alzheimer disease* and diabetic complications" [emphasis added].

Accordingly, applicants maintain that there is an art-recognized nexus between a model of amyloidosis in a mouse pancreas and a possible treatment for Alzheimer's disease.

#### **Summary**

Applicants maintain that the pending claims are in condition for allowance. Accordingly, allowance is respectfully requested.

If a telephone conference would be of assistance in advancing prosecution of the subject application, applicant's undersigned attorney invites the Examiner to telephone him at the number provided below.

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No fee, other than the enclosed \$430.00 sum, is deemed necessary in connection with the filing of this Amendment. However, if any additional fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,



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John P. White  
Registration No. 28,678  
Alan J. Morrison  
Registration No. 37,399  
Attorneys for Applicants  
Cooper & Dunham LLP  
1185 Avenue of the Americas  
New York, New York 10036  
(212) 278-0400